I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-63 as originally filed

Claims, No.:

1-53 as originally filed

Drawings, sheets:

1/24-24/24 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1, 3, 5-43, 46-53,

because:

☒ the said international application, or the said claims Nos. 1, 5-43, 46-53 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1, 3, 5-43, 46-53 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrialapplicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2,4
Inventive step (IS)	Claims	2,4

Industrial applicability (IA) Claims

2. Citations and explanations
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The subject-matter of claim 1 lacks clarity. Claim 1 relates to the "use of a penetrant", wherein the use of the penetran has not been defined. The expression "such droplets **then acting** as carriers for the transnasal administration of ..." is not directedly linked to the use of the penetrant. The fact that droplets which may be formed by a composition containing a penetrant (unclearly defined in claim 1) may then act as carriers does not define the use of the penetrant. If the penetrant is a composition formed by droplets this has not been defined in the claim.

2. The subject-matter of claim 3 lacks clarity. Claim 3 relates to the "use of a penetrant", wherein the use is not clearly defined. Moreover, it is unclear from the wording of the said claim as to whether the use of a penetrant is claimed or the use of a combination of penetrant and an active substance. Finally, it is also unclear whether the last sentence "and/or for use in the field of ...." relates to the medical use of the combination comprising the penetrant or is given as an alternative definition for the active substance.

3. Claims 5-43 lack clarity since their wording includes two categories (product and use) as alternatives. Therefore, the scope for which protection is sought by the said claims remains so unclear that no opinion on novelty and inventive step can be given of the subject-matter claimed therein.

   Claim 46 relates to a "method for generating a protective immuno response on a mammal by vaccinating the mammal with a vaccine according to one of claims 36-43. This multiple reference renders the scope of claim 46 unclear since the mentioned claims are not equivalent alternatives. The same applies to dependent claims 47-53.

   An analogous analysis applies to the subject-matter of claim 45, insofar as the pharmaceutical composition is defined as one of claims 5-43.

4. Claims 1, 3, 5-43, 46-53 relate to subject-matter considered by this Authority to be

covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. The following documents have been considered for the establishement of the present written opinion:

   D1 = EP 0 475 160 A
   D2 = WO 9817255 A (cited in the application)
   D3 = DE 4107152 A (cited in the application)
   D4 = DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US ALMEIDA A J ET AL: "Nasal delivery of vaccines." XP002107393 -& JOURNAL OF DRUG TARGETING, (1996) 3 (6) 455-67. REF: 125 JOURNAL CODE: B3S. ISSN: 1061-186X., XP002109107 Switzerland
   D5= WO 90 09385 A

2. The penetrant in the form of a minute fluid droplet and its use for the preparation of a pharmaceutical as defined in claim 2, and the pharmaceutical composition comprising the said penetrant as carrier as defined in claim 4, are known in the art (cf. D1 to D3). The expression "preferably a vaccine composition for transnasal administration" employed in claim 2 has no limitative character. Therefore the subject-matter claimed in claims 2 and 4 lacks novelty. On page 13 of the description of the present application it has been acknowledged that the penetrants according to the present application are known as carriers in pharmaceutical formulations.

3. The problem underlying the present application appears to lie in the preparation of pharmaceutical fomulation useful for the transnasal administration of active substances, antigens or allergens.

D1 to D3 discloses the use of the penetrants such as those of the present application as carriers for the non-invasive administration of active substances (eg. insuline), especially transdermal.

D4 shows the general teaching relating to the nasal delivery of vaccines. D4 demonstrates that generally known carriers systems such as liposomes, microparticles and nanoparticles may be employed with expectation of success for the transnasal administration. This is also shown by D5 which discloses lipid excipients useful for both nasal delivery and topic application. Therefore the subject-matter claimed in the present application does not involve an inventive step.

4. For the assessment of the present claims 2, 4 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.